UNITED STATES DISTRICT COURT EASTERN DISTRICT OF NEW YORK IN RE: PROPECIA (FINASTERIDE) PRODUCTS LIABILITY LITIGATION	Master File No.: 1:12-md-02331 MDL No. 2331
PAUL DAWSON, Plaintiff, v. Merck & Co., Inc, and Merck Sharp & Dohme, Corp., Defendants.	Case No. 1:12-cv-01876-BMC-PK

OPPOSITION TO DEFENDANTS' MOTION TO PRECLUDE THE EXPERT TESTIMONY OF PLAINTIFF'S EXPERTS, ABDULMAGED M. TRAISH, PH.D., IRWIN GOLDSTEIN, M.D., AND MAHYAR ETMINAN, PHARM.D., M.S.C.

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INTRODUCTION

This case involves Defendants' (Merck & Co, Inc. and Merck Sharp & Dohme Corp., collectively "Merck"**)** failure to warn that Propecia causes ongoing sexual dysfunction following discontinuation of use. Shortly after its launch, Merck obtained clear evidence that Propecia could—*and did*—cause long-term sexual dysfunction. For more than a decade, Merck hid that information from men (like Paul Dawson). [redacted][1] [redacted][2] [redacted][3]

In 2011—long before he became an expert in this case—Dr. Abdulmaged Traish published the first of *six* peer-reviewed studies in the JOURNAL OF SEXUAL MEDICINE chronicling the story of a young man who experienced permanent sexual dysfunction stemming from his use of Propecia and opining on a viable theory of biological mechanism of injury.[4] Today, some six years later, there are dozens of peer-reviewed publications establishing *both* a plausible biological pathway and epidemiological basis that Propecia causes persistent sexual dysfunction.

Merck claims these data amount to little more than "junk science" and asks the Court to strike Plaintiff's Expert Reports. Specifically, Merck argues the following:

> *Dr. Traish's Theory of Biological Plausibility:* Merck argues Traish's theory of biological plausibility is primarily flawed because he: a) relied on animal studies; that b) failed to correlate to an actual dose in humans. In making this argument,

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[1] *See Affidavit of Timothy J.* (*"Theodore E. Laszlo, Jr.* (*"Laszlo Aff."*), Ex. 1 at *607.)
[2] *Laszlo Aff.*, Ex. 2 at 43:5-49:15.
[3] *Laszlo Aff.*, Ex. 3 at *282; *Id.*, Ex. 4 at *631.
[4] *Laszlo Aff.*, Ex. 5. Traish, AM., *et al. Adverse Side Effects of 5a-Reductase Inhibitors Therapy: Persistent Diminished Libido and Erectile Dysfunction and Depression in a Subset of Patients.* J Sex Med 2011;8:872–884.

Merck *never* actually challenges Traish's opinion regarding the pharmacokinetics of finasteride, or the physiological pathway the drug takes to causes harm. In fact, Merck fails to tell this Court that Traish published *six* peer-reviewed articles *on this topic before* being retained in this case. Moreover, the substance of its argument is equally flawed because: a) courts routinely admit animal studies where they are—as here—buttressed by an actual biological pathway; and b) the dosing level is irrelevant given Merck's *own* documents evidence that once the enzyme is saturated (i.e. "turned off") additional amounts of the drug have no impact on outcomes.

Dr. Irwin Goldstein's ("Goldstein") use of Gray-Scale Imaging is not Flawed: Goldstein based his report, in part, on his objective findings that penile fibrosis is observable under gray-scale ultrasound imaging. In response, Merck argues that an unpublished abstract he cites in his report requires exclusion of *his entire* testimony. In doing so, Merck fails to establish that: a) gray-scale imaging is fundamentally flawed (a mighty task, indeed, given *its own expert* praised the virtue of gray-scale in peer reviewed literature *before* being retained by Merck); or b) that Goldstein is unqualified to interpret gray-scale data.

Dr. Mahyar Etminan's ("Etminan") Epidemiological Review: Finally, Merck argues the Court ought to exclude Etminan because his analysis: a) is biased given his work in other litigation; b) fails to rely on the Bradford-Hill criteria; and c) is predicated on bad-data. In doing so, Merck: a) ignores that Etminan was *recruited* by a colleague to co-author a study on finasteride *long before* he was retained in this case; b) that the *vast majority* of cases reject the contention an epidemiologist must perform a Bradford Hill assessment; and c) the purported errors Merck cites are largely speculative and merely go his conclusion, as opposed to the method he employed. More problematic for Merck, *nothing* in its argument even endeavors to discredit Etminan's meta-analysis—a concession that the opinion is reliable.

Each of these opinions is discussed at length below. But, in the end, the science underlying these claims is sound and ought to be presented to the jury.

FACTS

I. *MERCK'S OWN DOCUMENTS* ESTABLISH THAT PROPECIA CAUSES ON-GOING SEXUAL DYSFUNCTION FOLLOWING DISCONTINUATION OF USE.

A. The Regulatory Process and Merck's Understanding Propecia Could Cause Persistent On-Going Sexual Dysfunction.

Propecia was initially approved by the Food and Drug Administration ("FDA") on December 19, 1997, for the treatment of male pattern hair loss ("MPHL"). [redacted]

[redacted]

[redacted][5] Based in large part on this concern, Merck spent the better part of the next decade following the drug's launch to down-play its *own* internal knowledge that Propecia, in fact, causes long-term sexual dysfunction.

1. Merck recognized evidence of persistent sexual dysfunction long before it modified the Propecia label.

The initial Propecia label reported that SAEs ("Sexual Adverse Events"), including decreased libido, erectile dysfunction, and ejaculation disorder could occur while on drug. [redacted]

a. Merck uncovers proof of persistent sexual dysfunction post-use and does nothing to alert consumers or doctors.

[redacted]

[5] *Laszlo Aff.*, Ex. 6 at 75:9-75:22; Ex. 7 at *760. [redacted]

[redacted]

Id. (emphasis supplied). [redacted] None of this was reported in the label.

[6] [redacted] *Laszlo Aff.*, Ex. 15 at 83:4-84:19.

[redacted] Nonetheless, Merck submitted this language to FDA. *Id.*, Ex. 17 at *112. [redacted] *Id.* Ex. 15 at 45:3-45:15.

b. Merck further waters-down the risk of SAEs, inserting patently deceptive language regarding the risk of harm.

But Merck's deceit was not limited to its word-play in the 2002 label. On the contrary, it took steps to water-down the actual threat, injecting language in the label that it knew was misleading. Specifically, to water-down the risk of SAEs, Merck added the following language in the 2002 label: "The incidence of each of the above side effects decreased to ≤0.3% by the fifth year of treatment with PROPECIA." [redacted]

[redacted]

. *Id.*, Ex. 15 at 83:4-84:19.

2. Merck uncovers additional evidence of post-use SAE's; 2006 to 2008 the Proscar and European Union regulatory experience.

By 2006, Merck began facing increasing regulatory scrutiny from European regulators. That scrutiny ultimately resulted in a radical change to the European label, warning consumers of ongoing sexual dysfunction following cessation of use. [redacted]

See Laszlo Aff., Ex. 21 at *257 (emphasis supplied).[7] [redacted]

[7] Proscar is a 5mg dose of finasteride. It is the same chemically as Propecia.

[redacted] *Id.*, Ex. 1 at *607.

[redacted]

[redacted] *Id.*, Ex. 25 at *905.

3. Merck finally amends the U.S. Propecia label in April 2012.

[redacted]

Id. at 1 (emphasis supplied). [redacted]

For more than twelve years, Merck possessed data establishing SAEs in some men did not resolve following discontinuation. Despite this, it did nothing to change the label. [redacted]

[8] *Laszlo Aff.*, Ex. 26, Department of Health and Human Services FDA Pharmacovigilance Review, June 2011 at 1 (emphasis supplied).

[redacted]

II. AN OVERVIEW OF PLAINTIFF'S GENERAL CAUSATION EXPERT OPINIONS IN THIS CASE.

Defendants' motion challenges the opinions of three of Plaintiff's general causation experts. Specifically, it seeks to exclude the testimony of Traish who opines on the causal mechanism of injury; Goldstein who supplies clinical opinions on the diagnosis of penile fibrosis; and Etminan who identifies an epidemiological basis that Propecia can cause persistent sexual dysfunction post-use. The following is an executive summary of their respective opinions.

A. Dr. Traish and the Mechanism of Injury.

Traish is a steroid biochemist who has been on faculty at a top-tier medical school for nearly forty years. Prior to being retained as an expert, he published *six* peer-reviewed studies regarding the biological pathway Propecia takes to cause persistent ongoing sexual dysfunction. His core theory—*which Merck does not challenge*—is that finasteride inhibits a family of enzymes known as 5α-reductases ("5ARs") which are widely distributed throughout the body, and in particular, the male sexual organs and Central Nervous System ("CNS"). Finasteride acts by binding with the 5AR enzyme to inhibit the formation of dihydrotestosterone ("DHT")—DHT is one of the chief culprits leading to MPHL. The pharmacokinetics of finasteride are such that it is a nearly irreversible inhibitor of the 5AR enzyme with an incredibly slow rate of dissociation, leading to a long-lasting effect of the drug regardless of the dosage taken. In simpler terms, the drug binds to the receptor so tightly, it forms a bond that can last months before unbinding.[9] While

[9] *See Defs' Decl.*, Dkt. 54111-1, Ex. 2 at 18-29; *Laszlo Aff.*, Ex. 27 at 96:11-100:23; Ex. 28 at 1659-1665; and Ex. 29 at 157:19-158:14.

the drug binds to the receptor, the receptor is not available to assist in the normal biologic process of transforming testosterone to 5α-DHT, thus reducing DHT levels.

5α-dihydrotestosterone ("5α-DHT") plays a crucial role in erectile function; including regulation of blood flow in penile tissue via activation of nitric oxide synthase ("NOS"). Utilizing animal studies and basic scientific research evidencing how finasteride effects these hormones, the report concludes that finasteride ultimately decreases the production of 5α-DHT (which it is intended to do), and that, in turn, decreases expression and activation of endothelial ("eNOS") and neural ("nNOS") nitric oxide synthases. The absence of 5α-DHT results in the death of penile smooth muscle cells and increases formation of connective tissue leading to changes in penile tissue histology and architecture. The end result of this cascade is fibrosis (scarring) of the penile tissue. Fibrosis in the corpus cavernosum leads to poor tissue compliance and the inability of the corpus cavernosum to relax and expand—ultimately resulting in erectile dysfunction.

B. Goldstein and Clinical Observation of Penile Fibrosis.

Goldstein spent the better part of his career studying sexual dysfunction in men, including erectile dysfunction and its origins. Given his work in this arena, he first suspected finasteride was a potential cause of persistent sexual dysfunction in men more than a decade ago. For purposes of this litigation, Goldstein offered an opinion that finasteride can cause persistent suppression of 5AR which, in turn, leads to a state of androgen deprivation: a) causing biochemical changes in cavernosal tissue; b) impacting tissue material properties; and c) resulting in adverse clinical impacts stemming from these changes.

Additionally, Goldstein performed a retrospective case study of 37 individuals beginning in 2016. Using gray-scale ultrasounds, Goldstein identify evidence of penile fibrosis in Propecia-exposed individuals. Seeking confirmation of his findings, Goldstein sought a secondary opinion

from his colleague Dr. Bertolotto. In reviewing the same 37 individuals as Goldstein, Dr. Bertolotto agreed with Goldstein 84% of the time related to how he interpreted the images.

C. Dr. Etminan and his Epidemiological Review.

Long before he was retained as an expert in this case, Etminan was contacted by a colleague at Eli Lilly & Co., who was evaluating the relationship between finasteride and SAEs. *See Laszlo Aff.*, Ex. 57 at 160:5-161:19. Ultimately, Etminan collaborated with his co-author (Ali) to publish a paper evaluating the association between finasteride and Sexual Dysfunction ("SD") and Suicidal Ideation ("SI") in young men who used low-dose finasteride. Using MedDRA data, the study noted the presence of a safety-signal establishing an association between finasteride and persistent sexual dysfunction. [redacted] *Id.*, Ex. 22 at *920. [redacted] *Id.*, Ex. 25 at *905

After being retained by Plaintiffs, Etminan expanded his work to evaluate the Hazard Ratio ("HR") for SAEs and finasteride. Utilizing a large-scale insurance database, he identified treatment codes for persons who reported SD and finasteride use and compared the rate of these treatments versus a control group made up of persons who reported SD and used a drug with no known association to SD. Ultimately, he observed an HR of 1.62 (95% CI:1.14-2.29) and an adjusted HR comparing finasteride users to control with respect to the first use of an erectile dysfunction drug was 2.73 (95% CI:2.01-3.69). His research evidenced that there was no difference in the risk of SD within six months of stopping Propecia compared to the period before—suggesting the risk of SD continues after stopping the drug. Notwithstanding his disclosure that he was a paid expert in this litigation, his work was *still* accepted for publication in 2016 in the peer-reviewed journal

Pharmacotherapy. Etminan also conducted a meta-analysis of relevant literature which confirmed the pooled relative risk ("RR") for all SD was 1.77 (95% CI:1.21-2.58, Figure 1 of Etminan Report). When the analysis was restricted to erectile dysfunction, the RR soared to 2.54 (95 % CI:1.66-3.89, Figure 2 of Etminan Report). Similar results were observed in a meta-analysis conducted by Mella who observed a RR of 2.22 (95% CI:1.03-4.78). *Laszlo Aff.*, Ex 30 at 1141.

ARGUMENT

The general rule in the Second Circuit is that, "the rejection of expert testimony is the exception rather than the rule" and the "[s]tandard for admissibility of expert testimony is especially broad." *In re: Vitamin C Antitrust Litigation*, No. 05–CV–0453, 2012 WL 6675117 at *3 (E.D.N.Y. Dec. 12, 2012) (citing *Clarke v. LR Sys*., 219 F. Supp. 2d 323, 332 (E.D.N.Y. 2002)). In evaluating a Rule 702 motion, the district court enjoys "broad latitude" to determine whether an expert's opinion is reliable. *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 142 (1999). And, while it is necessary for the Court to evaluate the reliability of the expert's testimony, "the court's inquiry under *Daubert* focuses not on the substance of the expert's conclusions, but on the principles and methodology used to generate the conclusions." *See Clarke*, 219 F. Supp. 2d at 332. In other words, the key issue is *not* what conclusion the expert reached, but whether the expert employed a sound methodology to reach her conclusion. As the Second Circuit observed:

> Although expert testimony should be excluded if it is speculative or conjectural, or if it is based on assumptions that are so unrealistic and contradictory as to suggest bad faith or to be in essence an apples and oranges comparison, other contentions that the assumptions are unfounded go to the weight, not the admissibility, of the testimony.

Grand River Enters. Six Nations. Ltd. v. King, 783 F. Supp. 2d 516, 526 (S.D.N.Y. 2011) (quoting *Boucher v. U.S. Suzuki Motor Corp.*, 73 F.3d 18, 21 (2d Cir. 1996)).[10] Put another way, where the attack is predicated upon an expert's conclusion—as it is here—as opposed to *how* the expert reached his conclusion, then the testimony is admissible.

In short, the Court's role is not to take sides in a dispute between experts; it is the province of the jury to weight the credibility of an expert's conclusions. *Graham v. Playtex Products, Inc.*, 993 F. Supp. 127 (N.D.N.Y. 1998), is instructive. In *Graham*, a product liability case alleging toxic shock following tampon use, Playtex moved to exclude the experts' testimony. The experts formed their opinion by comparing the amount of toxins in *in vitro* tests for various tampon compositions and opined certain tampons were less likely to develop specific bacteria. *Id.* at 129-30. In response, Playtex argued that *in vitro* testing did not properly mimic the vaginal environment. *Id.* at 131. Notwithstanding the court's questions regarding the experts' methodology and observation the opinion was predicated on an "analytical gap" between the data and the conclusions, the court denied the motion noting: a) the conclusions were not *so* unreasonable as to require exclusion; and b) the absence of epidemiological data supporting the experts' test was not determinative. *See Graham*, 993 F. Supp. at 132 (citing *General Electric Co. v. Joiner*, 522 U.S. 136, 118 S.Ct. 512, 139 L.Ed.2d 508 (1997)). In reaching this conclusion, the Court observed the experts' "methodology [was] neither esoteric nor novel. Neither is it perfect. Perfection, however, is hardly the standard." *Id.* at 133. Accordingly, the court held, "The grounds for the expert's opinion merely

[10] *See also BIC Corp. v. Far E. Source Corp.*, No. 01–7074, 2001 WL 1230706, at *1 (2d Cir. Oct. 12, 2001); *CDR-Wantagh, Inc. v. Shell Oil Co.*, No. 07–CV–4497 (DRH)(ETB), 2011 WL 795865, at *10 (E.D.N.Y. Feb. 28, 2011); *Cohalan v. Genie Indus., Inc.*, No. 10 Civ. 2415, 2013 WL 829150, at *5 (S.D.N.Y. Mar. 1, 2013); *GlobalRock Networks, Inc. v. MCI Communications Services, Inc.*, No. 1:09CV1284(MAD/RFT), 2013 WL 1891303, at *17-18 (N.D.N.Y. May 06, 2013); *Encompass Advisors, Ltd. v. Unapen, Inc.*, No. 3:09CV1949(DFM), 2013 WL 6331157, at *3-4 (D. Conn. Dec. 5, 2013); *Tiffany (NJ) Inc. v. eBay, Inc.*, 576 F. Supp. 2d 457, 459 (S.D.N.Y. 2007); *Brown v. Columbia Recording Corp.*, No. 03 Civ. 6570 DABTHK, 2006 WL 3616966, at *4 (S.D.N.Y. Dec. 12, 2006); *Stevens v. Metso Paper, USA, Inc.*, No. 3:07cv735 (MRK), 2009 WL 10688031, at *2-3 (D. Conn. Sep. 25, 2009).

have to be good, they do not have to be perfect." *Id.* (quoting *In re Paoli R.R. Yard PCB Litig.*, 35 F.3d 717, 744 (3rd Cir. 1994) *cert. denied*, 513 U.S. 1190, 115, S.Ct. 1253 (1995)).[11]

By way of example, Merck's attack against Goldstein evidences this dichotomy. In that attack, Merck challenges his opinion which, in part, is predicated upon his review of gray-scale ultrasound images evidencing penile fibrosis. The gist of Merck's argument is that Goldstein got it wrong in interpreting the images. However, in leveling this attack Merck *does not* challenge: a) the reliability of ultrasound images to diagnosis penile fibrosis (nor could it given its own expert published at least one paper praising the virtue of gray-scale imaging);[12] or b) that Goldstein—a thirty-plus year practitioner—is *unqualified* to interpret ultrasound data. In other words, Merck is not truly arguing that gray-scale imaging is unreliable; it is arguing that Goldstein's review of that data is wrong. This type of argument—which is repeated throughout Merck's motion—is the stuff of cross-examination, which goes to the weight, as opposed to the reliability, of the opinions.

I. DR. ABDULMAGED TRAISH IS QUALIFIED TO TESTIFY AND HIS METHODOLOGY ESTABLISHING BIOLOGICAL PLAUSABILITY IS SOUND.

Traish principally opines on the mechanism of injury—i.e., he outlines the biological pathway establishing how finasteride can cause persistent sexual dysfunction post-use. In response, Merck argues his testimony is inadmissible because: 1) his qualifications are not sufficient to opine on biological plausibility; and 2) he failed to employ a sound methodology.

A. Traish is Indisputably Qualified to Testify.

[11] *See also Safrani v. Werner Co.*, No. 95 Civ. 1267(LBS), 1997 WL 729110, at *1 (S.D.N.Y. Nov. 24, 1997); *Lappe v. American Honda Motor Co., Inc.*, 857 F. Supp. 222, 228 (N.D.N.Y. 1994) (Hurd, M.J.) ("Daubert's narrow focus is on the admissibility of novel scientific evidence under Fed. R. Evid. 702."), aff'd, 101 F.3d 682 (2d Cir.1996).

[12] *Laszlo Aff.*, Ex. 31 Punjani, N., Stern, N., ***Brock, G.***, *Atypical – A Common Clinical Population That Remains Unrecognized* [Poster Presentation] at a recent Sexual Medicine Society of North America meeting in San Antonio, Texas] Western University, London, ON, Canada; *see also id.*, Ex. 32, Bertolotto A, Baert AL. Color Doppler US of Penis. Springer-Verlag, Berlin Heidelberg: 2010

While Merck concedes, "Here, none of the challenged witnesses is unqualified to serve as an expert *per se*" (*see Defs' Brief*, Dkt. No. 111 at 6) it implicitly challenges Traish's qualifications claiming his is "not a physician, has no medical training, and has never diagnosed or cared for men with sexual dysfunction." *Id.* at 12. Plaintiff now responds to this argument.

1. Traish has researched male hormones and their relationship with male sexual physiology for nearly forty years; he is qualified to testify.

A cursory review of Traish's background evidences he is clearly qualified to opine on biological plausibility. The author and co-author of more than 200 peer-reviewed publications—including *six* on finasteride's persistent side effects—Traish has worked in the field of male sexual science for more than forty years.[13] *See Defs' Decl*., Dkt. 111-1, Ex. 2 at 1; *see Laszlo Aff.*, Ex. 38. He has received numerous government-sponsored grants on topics including the physiology of penile smooth muscle, the role of neurotransmitters in penile erection, and the role of endothelium in human penile erection—all of which are relevant to this case. *Id.*, Ex. 39. He also received private funding to study the role of androgens in modulating nitric oxide synthase in erectile physiology which is expressly the subject of his opinions in this litigation. *Id*. In short, he has spent a lifetime studying, publishing, and teaching on the very subject Merck now claims is junk science.

2. Traish need not be a clinician to offer opinions in this litigation.

[13] *See Laszlo Aff.*, Ex. 33, 34, 35, 36, and 37. The articles include: ***Traish AM***, Melcangi RC, Bortolato M, Garcia-Segura LM, Zitzmann M. *Adverse effects of 5α-reductase inhibitors: What do we know, don't know, and need to know?* REV ENDOCR METAB DISORD. 2015 Sep;16(3):177-98; ***Traish AM***, Haider KS, Doros G, Haider A. *Finasteride, not tamsulosin, increases severity of erectile dysfunction and decreases testosterone levels in men with benign prostatic hyperplasia*. HORM MOL BIOL CLIN INVESTIG. 2015 Sep;23(3):85-96; ***Traish AM***, Morgentaler A. *Re: effect of finasteride on serum levels of androstenedione, testosterone and their 5α-reduced metabolites in men at risk for prostate cancer*. J STEROID BIOCHEM MOL BIOL. 2013 Nov;138:462; ***Traish AM***. *5α-reductases in human physiology: an unfolding story*. ENDOCR PRACT. 2012 Nov-Dec;18(6):965-75; ***Traish AM***, Hassani J, Guay AT, Zitzmann M, Hansen ML. *Adverse side effects of 5α-reductase inhibitors therapy: persistent diminished libido and erectile dysfunction and depression in a subset of patients*. J Sex Med. 2011 Mar;8(3):872-84; and ***Traish A***. *The Impact of the 5α-Reductase Inhibitors (5α-RIs) on Male Sexual Function and Psychological Well-Being*. CURR SEX HEALTH REP. Published online 26th of August 2015.

Despite conceding he is qualified, Merck makes a veiled statement suggesting he is not arguing, "[h]e is not a physician, has no medical training, and has never diagnosed or cared for men with sexual dysfunction." *See Defs' Brief*, Dkt. No. 111 at 12.[14] But this is not the standard in the Second Circuit. Expert opinions are permitted where the witness "is qualified as an expert by knowledge, skill, experience, training, or education," and the expert's "scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine the fact in issue." Fed. R. Evid. 702. District courts possess broad discretion to determine whether an expert is qualified and may conclude an expert is qualified to testify outside of her formal training or specialty.[15] The standards employed by the trial court in making this determination are "liberal and flexible."[16] The witness's qualifications do not need to be perfectly on point, and testimony is permitted where the witness's "educational and experiential qualifications in a general field closely related to the subject matter in question." *Davids v. Novartis Pharm. Corp.*, 857 F. Supp. 2d 267, 276 (E.D.N.Y. 2012).

Traish clearly satisfies this threshold. At the outset, his opinion evaluates the biological plausibility of whether finasteride can cause persistent sexual dysfunction. None of his testimony requires clinical or epidemiological experience. In fact, in a recent opinion the Ninth Circuit reached this exact conclusion rejecting the defendant's argument an expert could not testify on

[14] Plaintiffs offered Traish as an expert for the purpose of establishing a biologically plausible mechanism. At no time, was Traish intended to offer an opinion as to epidemiologic and clinical evidence. Merck's suggestion otherwise in their brief is misleading. As per the transcript, to the extent there was epidemiological or clinical information provided in his report, it was for background purposes. *Laszlo Aff.*, Ex. 29 at 285-286. Further, the agreement between counsel was that this discussion *would not be* the basis of a *Daubert* challenge to Traish's opinions.

[15] *See generally See Hilaire v. DeWalkIndus. Tool Co.*, 54 F. Supp. 3d 223, 234 (E.D.N.Y. 2014); *Sorto–Romero v. Delta Intern. Machinery Corp*., 05-CV-5172, 2007 WL 2816191, at *4 (E.D.N.Y. Sept. 24, 2007); *United States v. Feliciano*, 223 F.3d 102, 120 (2d Cir. 2000); *Palazzetti Import/Export, Inc. v. Morson*, No. 98 CV 722, 2001 WL 793322, at *2 (S.D.N.Y. July 13, 2001).

[16] *Hilaire*, 54 F. Supp. 3d at 234 (quoting *Houlihan v. Marriott Int'l, Inc.*, No. 00 CV 7439, 2003 WL 22271206, at *3 (S.D.N.Y. Sept. 30, 2003)); *Krause v. CSX Transp.*, 984 F. Supp. 2d 62, 73-74 (N.D.N.Y. 2013) (explaining that to assess "whether a proposed expert is 'qualified,' the trial judge should remember the liberal purpose of Fed. R. Evid. 702, and remain flexibl[e] in evaluating the proposed expert's qualifications") (internal citations omitted).

biological plausibility in the absence of epidemiological evidence. *See Wendell v. GlaxoSmithKline LLC*, 858 F.3d 1227, 1233-38 (9th Cir. 2017). Thus, the question for this Court is whether he is qualified to testify about what happens to finasteride biologically when consumed by humans. The answer to that question is that he most assuredly is. For example, he was trained as a biochemist with a focus on steroid and hormone biology. *See Laszlo Aff.*, Ex. 29 at 77:8-78:5. He underwent a post-doctoral fellowship at the Boston University Medical School, and has been on faculty at the medical school for nearly forty years focusing his work on male sexuality. *Id.*, Ex. 38. He has taught in the medical school and has on *six* separate occasions published peer-reviewed articles discussing how finasteride biologically interacts with the body. And, in fact, Merck's contention that his absence of clinical experience somehow disqualifies him is overshadowed by the fact it too offers a non-medical Ph.D. to opine on biological plausibility (*see, e.g.*, Dr. Donald Pfaff, Ph.D. Expert Report). A scientist, specifically a scientist who is on the faculty of a top-tier medical school, and who has done research in this area for decades is qualified to offer opinions in this case regardless of whether he is a clinician and licensed medical doctor.

B. Traish's Opinions are Predicated Upon the Necessary Rigor and Sound Methodology Required to Satisfy Daubert.

The *Daubert* requirements are not set in stone and are well known to this Court. Generally, an expert may testify:

> If scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert by knowledge, skill, experience, training, or education, may testify thereto in the form of an opinion or otherwise.

Fed. R. Evid. 702. In evaluating this standard the court may consider the factors set forth in *Daubert* and its progeny, including whether the methodology can be tested, whether it was peer-review and published, has a known error rate, and is generally accepted in the field.[17]

1. Traish's six peer-reviewed publications evidence the rigor required to testify.

There is little doubt that Traish's analysis in the cases mirrors the rigor he employs in his day-to-day work. At the outset, on no less than *six* separate occasions Traish's work *on finasteride* was accepted for publication in some of the leading peer-reviewed journals in his field.[18] Most notably, in 2011, the JOURNAL OF SEXUAL MEDICINE—one of the preeminent journals in the field of sexual medicine—published *Adverse side effects of 5α-reductase inhibitors therapy: persistent diminished libido and erectile dysfunction and depression in a subset of patients.*[19] That paper theorized that finasteride saturated the 5-AR enzyme, resulting in decreased DHT production which, in turn negatively impacted NOS expression in the penis causing penile fibrosis. This is the very theory he advances here. When asked why he wrote his first article, he responded: "I am a steroid biochemist interested in the role of hormones and sexual function." *See Laszlo Aff.*, Ex. 29 at 58:18-20. Given his natural interest in this area of research, he continued to analyze the plausibility of persistent sexual dysfunction following discontinuation of finasteride, publishing additional articles in 2012, 2013, and 2014. In *Daubert II* the Ninth Circuit noted:

> That the research is accepted for publication in a reputable scientific journal after being subjected to the usual rigors of peer review is a significant indication that it is taken seriously by other scientists, i.e., that it meets at least the minimal criteria of good science.

[17] Plaintiff reincorporates by reference this section throughout the brief. It is set forth here to outline the factors the court may consider in evaluating an expert's opinion. *See generally Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 113 S.Ct. 2786, 2797 (1993); *see also Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146, 118 S.Ct. 512 (1997); *Kumho Tire Co. Ltd. v. Carmichael*, 119 S.Ct. 1167 (1999).
[18] *Supra* fn. 13. Traish testified his publications form the basis for his opinions. *See Laszlo Aff.*, Ex. 29 at 57:9-17.
[19] *Supra* fn. 13.

Daubert v. Merrell Dow Pharmaceuticals, Inc. ("*Daubert II*"), 43 F.3d 1311, 1318 (9th Cir.1995). Traish's publications satisfied the rigors of the peer-review process *six* times; they satisfy *Daubert*.

But, his publications were far from the totality of the work he completed in this case. Once he became interested in finasteride-related injuries, he reviewed an enormous amount of literature. Exhibit B to his report contains a list of approximately 700 published articles that he reviewed and considered in forming his opinions. *See Laszlo Aff.*, Ex. 29 at 55:13-24. Notably, Traish is not only trained in urology and sexual medicine, but also teaches medical students how to critically review information and publications in the medical literature. *Id.*, Ex. 29 at 85:24-86:4. The foundation he laid to complete his work far exceed the standard for admissible expert testimony.

2. Traish's opinion is not a litigation-driven opinion given he published it in the medical literature before he was retained as an expert.

Traish's first peer-reviewed publication on the relationship between finasteride and persistent side effects was published in 2011. *Supra* at fn. 13. His original paper began to form the building blocks for his opinion in this case that finasteride can cause persistent sexual dysfunction. That original paper marked the starting point for six peer-reviewed articles, dozens of lecturers,[20] and countless review of peer-reviewed material—all of which was done *before* he agreed to testify.

Plaintiff retained Traish in January 2016, long after he began researching in this field. *See Laszlo Aff.*, Ex. 29 at 38:25-40:4. While part of a reliability analysis evaluates potential litigation bias, the crux of Traish's opinions were generated before he was retained. As such, there is no

[20] *Laszlo Aff.*, Ex. 40(a)-(e), Traish PowerPoints: Traish, A.M., 5α-Reductase in Human Physiology: An Unfolding Story (2011); Traish, A.M., The Biology of 5α-Reductase: An Unfolding Story; Traish, A.M., Effects of Finasteride on Sexual Function. 38th Annual Conference, American Society of Andrology (2013); Traish, A.M., Post-Finasteride Syndrome: "Fact or Fiction." Sexual Medicine Society of North America (2013); Traish, A.M., Persistent Sexual Symptoms After 5 α-RI (Finasteride, Duasteride) Treatment is Significant Health Issue for Men. Endocrine Form, AUA (2014); Traish, A.M., 5α-Reductase Inhibitors therapy is Associated with Risk of Sexual Dysfunction. 7th International Meeting Steroids and Nervous System (2013).

litigation bias, and given the articles' acceptance in well-credentialed journals, the opinions in those papers—consistent with his opinions here—are the stuff of good science *Daubert* requires.[21]

3. Traish's opinions rest on a reliable foundation and methodology.

In challenging Traish's methodology, Merck levels four independent attacks. They are: 1) animal studies are not reliable; 2) the dose used in the animal studies in inconsistent with that used in humans; 3) one of the animal studies used dustasteride (another drug in the 5AR family); and 4) his report is unreliable because it fails to point to human testing to establish fibrosis.

a. Critique No. 1: An expert may rely on animal studies.

At the outset, nothing in this argument truly challenges Traish's theory evaluating the physiologic pathway from finasteride ingestion to injury, which in and of itself is sufficient to satisfy *Daubert*. Instead, Merck contends his opinion is flawed because it relies—in part—on animal modeling. For example, in Zhang, a group of researchers analyzed the impact of finasteride on rats.[22] Ultimately, the rats were sacrificed at the end of the study and their penis' were biopsied to evaluate what, if any impact, finasteride caused. The clear, and undisputed findings of the study was that finasteride did, in fact, result in significant penile scarring. As the authors described:

> Long-term 5ARI treatment did attenuate the erectile function of aged rats. The mechanisms might have been the decreased rate of autophagy and an increased rate of apoptosis in the cavernous smooth muscle cells, suggesting a new role for androgen in maintaining the structural and functional integrity of the erectile organ.

Id. Similar results were observed by Pinksy and Oztekin.[23] Relying, in part, on these studies, Traish's report uses these findings to support his theory that DHT deprivation results in a cascade

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[21] *McClellan v. I-Flow Corp*., 710 F. Supp. 2d 1092, 1127 (D. Oregon 2010) (allowing testimony despite plaintiff's counsel's extensive role in drafting expert report).

[22] *See Defs' Decl.*, Dkt. No. 54111-1, Ex. 38 (Zhang MG, Wang XJ, Shen ZJ, Gao Pl *Long-term oral administration of 5alpha-reductase inhibitor attenuates erectile function by inhibiting autophagy and promoting apoptosis of smooth muscle cells in corpus cavemosum of aged rats*. UROLOGY 2013 ;82:743 e9-15).

[23] *See Defs' Decl.*, Dkt. No. 54111-1, Ex. 36 and 37 (Pinsky MR, Gur S, Tracey AJ, Harbin A, Hellstrom WJ. *The effects of chronic 5-alpha-reductase inhibitor (dutasteride) treatment on rat erectile function*. J Sex Med.

effect leading to penile fibrosis. *See Defs' Decl.*, Dkt. No. 111-1, Ex. 2 at 38-49. Specifically, Traish outlines a mechanism whereby the downstream effects of interfering with the production of DHT leads to alterations in levels of nitric oxide synthase which leads to fibrosis, or scarring, of the penile tissue. The science underlying Traish's opinions on the biologically plausible mechanism, including animal studies, are sound science on which to base his opinion.

Merck, in turn, seeks to exclude his testimony predicated on his reliance on animal modeling studies. But that is not the law in this Circuit. Specifically, courts in this Circuit have found that the "existence of a biologically plausible mechanism bolsters the reliability of the proffered opinions on causation." *See In re Fosamax Prod. Liab. Litig.*, 645 F. Supp. 2d 164, 183 (S.D.N.Y. 2009). This is particularly true in pharmaceutical and toxic tort cases where experts routinely rely on animal models and bench science to support their opinions on biologically plausible mechanisms of injury. *See McMillan v. Togus Regional Office, Dept. of Veterans Affairs*, 294 F. Supp.2d 305, 311-12 (E.D.N.Y. 2003) ("Because many of the chemical exposures associated with diseases in humans have been confirmed in experimental studies, data derived from such [animal] studies are generally accepted as a valuable guide in the assessment of biologic plausibility."). The primary reason for this is because ethical constraints preclude researchers from conducting experiments where the study's end-point is harm to the patient.[24] In fact, Traish explained, he teaches his students that *in vitro* and animal studies are critical to clinical medicine,

2011;8:3066-3074; and Oztekin CV, Gur S, Abdulkadir NA, et al. *Incomplete recovery of erectile function in rat after discontinuation of dual 5-alpha reductase inhibitor therapy*. J Sex Med. 2012;9:1773-1781).

[24] *See, e.g.*, *In re Zicam*, 2011 WL 798898, at *8 (quoting Fed. Judicial Ctr., *Ref. Man. On Scientific Evid.* 405 (2000)) (noting "because it 'is often unethical to experiment on humans by exposing them to known doses of chemical agents, animal toxicological evidence often provides the best scientific information about the risk of disease from a chemical exposure.'"); *see also In re Rezulin Product Liability Litig.*, 369 F. Supp. 2d 398, 406 (S.D.N.Y. 2005) (noting that although the clinical trial is the "gold standard" for determining causation, such studies are not always available when ethical constraints preclude exposing human beings to agents known to be toxic).

"[b]ecause without translational research, we don't go anywhere." *See Laszlo Aff.*, Ex. 29 at 94:1-2. In short, animal modeling is ubiquitous and accepted in medical research.

In order to develop an opinion on the biologic plausibility, experts utilize many sources. THE REFERENCE MANUAL ON SCIENTIFIC EVIDENCE (THIRD), specifically notes in the context of a toxic tort, such as here with exposure to finasteride, "summing, or synthesizing, data addressing different linkages [between kinds of data] forms a more complete causal evidence model and can provide the biological plausibility needed to establish the association" being advocated or opposed. *See* REFERENCE MANUAL ON SCIENTIFIC EVIDENCE (THIRD) Sec. II.A (2011) (citing *Institute of Medicine and National Research Council, Dietary Supplements: A Framework for Evaluating Safety* 262 (2005)). The IARC reached a similar conclusion noting that "[t]he final overall evaluation is a matter of scientific judgment reflecting the weight of the evidence derived from studies in humans, studies in experimental animals, and mechanistic and other relevant data." *Id.* For this reason, courts routinely allow experts to rely upon animal modeling as long as there is a basis for the extrapolation from animal studies to humans. *See In re Fosamax*, 645 F. Supp. 2d at 186-87. These courts reason that animal studies may be admissible when the "gap between what these sources reasonably imply and more definitive scientific proof of causality is not too great," and when "the inferences are of a kind that physicians and scientists reasonably make from good but inconclusive science." *See generally In re Ephedra Prods. Liab. Litig.*, 393 F. Supp. 2d 181, 197 (S.D.N.Y. 2005). When animal studies are admissible, the expert's "Extrapolation from studies to support [her] conclusions, as well as [her] use of *in vitro* versus *in vivo* studies [goes] to the weight and not the admissibility of expert testimony." *In re: Mirena IUD Prod. Liab. Litig.*, 169 F. Supp.3d 396, 432 n.23 (S.D.N.Y. 2016) (citing *In re Ephedra*, 393 F. Supp. 2d at 189). In

short, the fact an expert utilizes animal modeling to render an opinion *is not*, in and of itself, a basis to exclude the expert.

Recently, in *K.E. v. GlaxoSmithKline LLC*, (a case alleging Paxil caused birth defects in an unborn fetus), the court, while recognizing the limitations of animal studies, allowed the expert to testify noting any limitations is "best addressed with precautionary instructions to the jury and rigorous cross examination." *K.E. v. GlaxoSmithKline LLC*, No. 3:14-CV-1294(VAB), 2017 WL 440242, at *11 (D. Conn. Feb. 1, 2017), *appeal withdrawn sub nom. K. E. v. SmithKline Beecham Corp.*, No. 17-618, 2017 WL 3911570 (2d Cir. June 14, 2017) (citing 1-4 Drug Product Liability § 4.04). Ultimately, the *K.E. Court* concluded that disallowing expert testimony based on the purported flaws in animal studies places an overly burdensome standard on plaintiffs holding:

> Given the liberal thrust of the Federal Rules of Evidence, the flexible nature of the *Daubert* inquiry, and the proper roles of the judge and the jury in evaluating the ultimate credibility of an expert's opinion, we do not believe that a medical expert must always cite published studies on general causation in order to reliably conclude that a particular object caused a particular illness . . . . To so hold would doom from the outset all cases in which the state of research on the specific ailment or on the alleged causal agent was in its early stages.[25]

Id. (citing *Heller v. Shaw Indus., Inc.*, 167 F.3d 146, 155 (3d Cir. 1999)). Such is the case here. Specifically, concerns regarding Traish's reliance on animal studies are satisfied *vis-à-vis* proper jury instructions and vigorous cross-examination.

Drake v. Allergan, Inc., 111 F. Supp. 3d 562, 570–71 (D. Vt. 2015), appeal dismissed (Nov. 12, 2015), is also instructive. In that case, the defendant—as Merck does here—argued the expert's reliance on animal studies required the court exclude his opinion. The district court rejected this

[25] Indeed, in the cases where courts exclude expert testimony on this basis, it was because the expert could not provide an opinion on why it was appropriate to use an animal model. For instance, Merck cites the *Mirena* litigation to support its contention that animal studies are inadmissible. But a careful review of that case does not stand for that proposition. Instead, in that case Judge Sibel rejected the expert's opinion because, unlike here, the expert merely copied and pasted portions of studies to support his opinion without any analysis. In short, the expert did not link the studies to any independent analysis so as to support his theory, and as such, his conclusion was "too great an analytical leap." *In re Mirena IUD Prod. Liab. Litig.*, 169 F. Supp. 3d 396, 445 (S.D.N.Y. 2016).

argument allowing the expert to testify on biological plausibility based upon animal studies where the expert's report "[d]escribe[ed a] potential mechanisms of how Botox might spread, including to the brain, further support an inference of biologic plausibility." *Id.* at *570. The *Drake* Court was also persuaded by the fact the plaintiff's evidence included acknowledgment by an Allergan employee of the risk. [redacted]

Id., Ex. 21 at *257 (emphasis supplied). In fact, *nothing* in Merck's motion actually claims that Traish's proposed biological pathway is incorrect. Taken collectively, these admissions, coupled with the absence of any challenge to his biomechanical theory justify his use of animal studies.

b. Animal studies are the long-recognized method to perform mechanistic studies.

Similarly, Merck fails to identify any basis that the animal studies were done incorrectly. Merck's brief notes the animal experiments were performed as follows:

> Animals 'had their cavernosal nerves electrically stimulated during anesthesia; the rats were killed; their penises were dissected from their bodies; the cavernosal tissue of the penis was excised into strips, treated chemically in various organ baths, and electrically stimulated. The researchers then examined relaxation of the smooth muscle in the tissue strips.

Defs' Brief, Dkt. No. 111 at 14. As Traish testified, this is the well-established and validated method to use in *in vitro* experiments on penile tissue. *See Laszlo Aff.*, Ex. 29 at 247:16-248:1. This opinion was predicated on his own experience running a lab utilizing animal studies for nearly forty years. According to Traish, these are "well-done" studies that provide reasonable evidence the same outcome would occur in humans. *Id*. at 205:21-25. "Just because we did not cut someone's else's penis and did the study, that does not mean it's unlikely that this happens." *Id.* Nothing in Merck's motion challenges this proposition.

Further, Merck's own experts endorse animal models as the proper way to evaluate erectile dysfunction. At least two of Merck's primary experts (Dr. Brock and Dr. Mulhall) have relied upon animal modeling in their own independent research. [26] In fact, in 2011—before being retained in this case—Dr. Brock wrote: "While the complex nature of human sexual function cannot possibly be replicated fully, *the use of animal models provides a valid alternative* to the investigation and

[26] *Laszlo Aff.*, Ex. 42, Kovac JR, DeYoung L, Lehmann KJ, § E, ***Brock GB***. *The effects of combined free radical scavenger and sildenafil therapy on age-associated erectile dysfunction: An animal model*. UROL ANN. 2014 Oct;6(4):314-20; *Id.*, Ex. 43, Chung E, Garcia F, Young LD, Solomon M, ***Brock GB.*** *A comparative study of the efficacy of intralesional verapamil versus normal saline injection in a novel Peyronie disease animal model: assessment of immunohistopathological changes and erectile function outcome*. J UROL. 2013 Jan;189(1):380-4; *Id.*, Ex. 44, Chung E, De Young L, ***Brock GB***. *Rat as an animal model for Peyronie's disease research: a review of current methods and the peer-reviewed literature*. INT'L LMPOT RES. 2011 Nov-Dec;23(6):235-41; *Id.*, Ex. 45, ***Mulhall JP***, Verma N, Deveci S, Tal R, Kobylarz K, Muller A. *Sildenafil citrate improves erectile function after castration in a rat model*. BJU INT. 2014 Apr;113(4):656-61.

evaluation of sexual dysfunction. *Id.*, Ex. 46 at 3291-305.011 (emphasis supplied). The use of animal modeling to correlate to human experience is widely accepted in the medical community.

c. Critique No. 2: The dose used in the animal studies does not make it unreliable.

Merck also attacks Traish's reliance on animal studies claiming the administered dose of finasteride and dutasteride are not relevant to human consumption. In fact, at his deposition Merck's counsel went so far as to describe it as a "whopping dose." *See Laszlo Aff.*, Ex. 29 at 240:19-21. In response, Traish explained the dose was irrelevant because, "[w]hat's important is that with this dose, you suppress the DHT to a basic level. Given the fact that once you saturate the enzyme, once the enzyme is fully occupied by the inhibitor, the rest is irrelevant. How much is out there is basically irrelevant, unless its toxic." *Id.*, Ex. 29 at 241:16-22. When pressed about the dose of the animal studies, Traish repeated his answer:

> I go back to the biology. Because the enzyme is saturated at around .2 milligram, it doesn't matter at this point whether this dose is three times or five times or ten times. The enzyme is saturated at that level dose, and once the enzyme is saturated and the inhibition of DHT took place, I expect some of these biological effects will be similar, you know, irrespective of that dose.

Id. at 254:12-20. In other words, once the enzyme is saturated it is effectively "shut off"—meaning that the presence of additional finasteride does not somehow provide an additional downstream effect. The analogy Traish drew was to a room with ten seats. "Once these ten seats are occupied, it doesn't matter how many other people are standing out there, only ten people can sit." *Id.* at 162:9-13. And, in fact, Merck's own internal documents support the fact that once the enzyme is saturated additional amounts of the drug will produce no additional effect because the enzyme is already impacted. *See Defs' Decl.*, Dkt. No. 111-1, Ex. 2, Sec 4.4. at 26. Merck does nothing to challenge this theory, nor could it given the fact it agrees that Propecia is expressly *designed* to

saturate the enzyme (i.e., stop it from producing DHT). As such, the mere fact the researchers used a "whopping" dose does not undermine their results that 5ARs cause penile fibrosis.

d. Critique No. 3: Dutasteride is sufficiently reliable to extrapolate to finasteride.

The next attack on Traish's reliance on animal studies is that some of them use dutasteride instead of finasteride. First, this is plainly misleading given the first study (Pinsky) utilized dutasteride and the next two (Zhang and Oztekin (*supra* fn. 23)) used finasteride to confirm the same effect. Second, these are downstream effects from drugs in the same class. Dutasteride and finasteride are members of the same class of drugs that inhibit the 5AR enzyme. *See Laszlo Aff.*, Ex. 29 at 237. Accordingly, Traish testified that the data from dutasteride can be applied to finasteride due to the similar biological effects of the drug. *Id.* at 223, 254:7-257:5. In fact, both drugs work to inhibit the conversion of testosterone to DHT. These studies involve a complex biochemical cascade of effects that demonstrate an ultimate result of inhibiting NOS. There is no evidence to suggest that any difference between the drugs changes the cascade of biological events that follow. Stated simply, while there may be differences in the way the drugs are absorbed, metabolized, or distributed in the body due to the different pharmacokinetics, the ultimate pharmacodynamics effect—inhibiting formation of DHT—is the same. And as such, the biological cascade that results from that effect is necessarily the same.

e. Critique No. 4: Human histology studies on penile tissue in this instance is impossible.

Finally, Merck contends the absence of histology done on human penile tissue to confirm the mechanism of injury is fatal to Traish's opinion. It is unethical to do studies on a mechanism of injury where the study could result in harm to a human. *See Laszlo Aff.*, Ex. 29 161:10-17; Ex. 27 at 174:15-24; *see also* REFERENCE MANUAL ON SCIENTIFIC EVIDENCE (THIRD) Sec. II.C (2011)

(noting it is unethical to conduct human testing where the endpoint is a known harm). Here, in order to do a human study, a man would need to be given a drug with a known side effect of sexual dysfunction. Then, once the sexual dysfunction begins, consent to remove his penile tissue. There is simply no way an IRB would approve the study. And even if approved, obtaining enough men to consent to potential long term sexual dysfunction and the promise of a penis biopsy would place serious impediments to enrollment in the clinical trial. Because it is unethical to experiment on humans by exposing them to harmful doses of chemical agents, animal toxicological evidence often provides the best scientific information about the risk of disease from a chemical exposure.[27] THE REFERENCE MANUAL ON SCIENTIFIC EVIDENCE (THIRD) also notes that animal studies often provide useful information about pathological mechanisms and play a complementary role to epidemiology. *Id.* Sec. II.C (2011).

Recognizing these ethical constraints, Merck nonetheless suggests that it is still possible to obtain pathology and that the experts in this case *chose* not to do so. This is, at best, a stretch. Specifically, Merck cites a study (Gupta) that analyzed penile pathology following penile implant surgery noting the penile tissue was removed and analyzed. *See Laszlo Aff.*, Ex. 47 at 159-63; Ex. 29 at 202:8-204:24. But Gupta is not remotely analogous to this case. In Gupta the tissue was *already* being removed during a separate surgical procedure (penile implant surgery). As such, it was possible to collect human tissue due to the underlying surgery. As Traish explained, "we take the tissue left over from the pathology, which the pathology will throw out, and we use it to do experiments." *Id.*, Ex. 29 at 199:19-200:12. Taking human tissue that is left over from an agreed-to surgical procedure is not remotely analogous to asking men to consent to a penile punch-biopsy.

[27] *See, e.g.*, Office of Tech. Assessment, U.S. Congress, Reproductive Health Hazards in the Workplace 8 (1985); Ref Manual of Sci Evi, Third, at 639; *In re Rezulin Product Liability Litig.*, 369 F. Supp. 2d 398, 406 (S.D.N.Y. 2005) (noting that although the clinical trial is the "gold standard" for determining *causation*, such studies are not always available when ethical constraints preclude exposing human beings to agents known to be toxic).

4. Whether fibrosis may be reversible in some men is not relevant, does not impact the causation analysis and merely goes to damages.

Finally, Merck contends that Traish cannot testify because he cannot prove that fibrosis is permanent. *Defs' Brief*, Dkt. No. 111 at 17. This argument completely misses the mark and is wholly irrelevant to whether Propecia causes *persistent* sexual dysfunction post-use. At the outset, Traish testified that in his opinion the fibrosis caused by finasteride *may* be irreversible. *See Laszlo Aff.*, Ex. 29 at 278:23-281:7. [redacted] Traish's theory is that *persistence* can occur. That persistence can, in some men, be permanent. In fact, Traish clarified that while fibrosis may be reversible, that is not true in all cases. *Id.* 279:9-10. Merck's counsel tried to suggest all fibrosis, including any caused by finasteride is reversible, but Traish testified that there are many types of fibrosis, and that at this point in time, it is not known whether fibrosis caused by finasteride is reversible or not, and would depend on many factors including the nature and length of the fibrosis. *Id.* at 281:3-7.

Moreover, even assuming Merck is correct—i.e., that at some point in time a man's symptoms will resolve—that argument has *nothing* to do with causation. Instead, it has to do with the sufficiency of the label (i.e., whether telling men: "[r]esolution occurred in ***all*** men who discontinued therapy with PROPECIA due to these side effects. . . .") should be inferred to mean resolution could take days, weeks, months, or even years. *See, e.g.*, *In re Fosamax Prod. Liab. Litig.*, No. 06 MD 1789(JFK), 2013 WL 3326821, at *3 (S.D.N.Y. July 1, 2013) (holding the sufficiency of a label is a factual determination for the jury); *Billiar v. Minnesota Min. and Mfg. Co.*, 623 F.2d 240, 247 (2d Cir.1980) (same). Whether a man's symptoms resolved years after discontinuing use does not undermine Traish's theory on *how* finasteride creates a cascade effect leading to fibrosis. It merely impacts the amount of time the man experiences harm (i.e., it relates

solely to damages). Merck has not established Traish's theory lacks a sound scientific basis; its motion to exclude ought to be denied.

II. DR. IRWIN GOLDSTEIN'S CLINCAL OBSERVATIONS AND USE OF GRAY-SCALE ULTRASOUND IS RELIABLE.

Goldstein is a Clinical Professor of Surgery at the University of California at San Diego ("UCSD") and the Director of the San Diego Sexual Medicine. Goldstein received an Sc.B from Brown University with honors in biomedical engineering in 1971 and an M.D.C.M. from McGill University Faculty of Medicine in 1975. In 2004, he was appointed to serve as the President of the Institute for Sexual Medicine in San Diego, California. He has treated patients with sexual dysfunction in his private practice at the UCSD since 2007. He previously served as the President of the Sexual Medicine Society of North America and as a member of the board of the International Society for Sexual Medicine. He served as the editor in chief for the JOURNAL OF SEXUAL MEDICINE, is the current editor in chief for the SEXUAL MEDICINE REVIEWS, and has authored over three-hundred peer-reviewed medical and scientific journal articles. He performs research in the area of testosterone and erectile dysfunction, as well as the clinical assessment and treatment of sexual dysfunctions in men. *See Defs. Decl.*, Dkt. No. 111-1, Ex. 4 and 5.

A. Focusing on the Minutia of Goldstein's Conclusions, Merck Entirely Ignores a Substantial Majority of His Report.

Goldstein's Expert Report comprises sixty-one paragraphs covering over twenty pages. *See Defs. Decl.*, Dkt. No. 111-1, Ex. 4. His conclusions are, in part, based upon clinical studies "supportive of and consistent with the hypothesized mechanisms of PFS and its persistence after discontinuation of finasteride treatment." *Id.* at 54. Yet, Merck focuses *solely* on *only five paragraphs* (i.e., at 49-53) in an attempt to exclude *all* of his testimony. In short, Merck foists upon the Court the novel proposition that Goldstein's entire opinion, based on a variety of *independent sources*, should be ignored because of his retrospective abstract (which used

ultrasound imaging to confirm, clinically, the existence of penile fibrosis in a subset of his Propecia-patient population). This has no basis in law or fact. To be clear, Goldstein's case study is nothing more than a means to confirm the clinical results and biological evidence proffered by other clinicians. *Id.* at 54-57.

In the *early 2000s*, and long before this litigation began, Goldstein formulated the following opinion:

> In my opinion, Propecia is a drug that causes a sustained and prolonged lowering of dihydrotestosterone to a young patient with androgenic alopecia typically, that this insult causes phenotypic changes to the erectile tissue of that person. *And those phenotypic changes, which are multiple*—by the way, they also cause phenotypic changes to the prostate of that person—*lead to alteration of erectile function by increasing the fibrotic quality of the erectile tissue*.

Id., Ex. 27 at 145:11-25 (emphasis supplied). While Merck appears to portray Goldstein's recent case study as the basis for his penile fibrosis theory, the earliest ultrasound taken for the case study was in 2016—over decade after he began formulated his opinions regarding Propecia and penile fibrosis. *Id.*, Ex. 48 at 529:16-19; Ex. 49 and 50. In other words, Merck posits that the entirety of Goldstein's opinion regarding penile fibrosis should be excluded because of one case study he conducted over a decade after reaching his conclusions. The case study is not the basis for Goldstein's penile fibrosis theory, nor was that ever its intent.

1. Goldstein's review of and reliance on peer-reviewed studies in confirming the symptoms realized in his patient population cannot be excluded under Daubert and must be left to cross-examination.

Generally, the factual basis of an expert's opinion goes to the credibility of the testimony, not the admissibility, and it is up to the opposing party to examine the factual basis for the opinion in cross-examination. *U.S. Bank Nat. Ass'n. v. PHL Variable Life Ins. Co.*, 112 F. Supp. 3d 122, 134 (S.D.N.Y. 2015) (internal citations omitted). Importantly,

> Mere weakness in the factual basis of an opinion *bears on the weight of the evidence, not its admissibility. Burke v. TransAm Trucking, Inc.*, 617 F. Supp. 2d

> 327, 335 (M.D. Pa. 2009); *see also Phillips v. Raymond Corp.*, 364 F. Supp. 2d 730, 743 (N.D. Ill. 2005). Only if the expert's opinion is so fundamentally unsupported that it can offer no assistance to the jury must such testimony be excluded. *Boykin*, 2015 WL 539423, at *6.

U.S. Bank Nat. Ass'n., 112 F. Supp. 3d at 134 (emphasis supplied). *Phillips* is instructive. In *Phillips*, a biomechanical engineering expert's methodology was challenged as nothing more than *ipse dixit*. 364 F. Supp. 2d at 743. As part of her research, the biomechanical engineer reviewed "a considerable amount of medical literature" in addition to various categories of documents related to the accident. *Id.* In disagreeing that the expert's methodology was mere *ipse dixit*, the Court stated, "the process of analyzing assembled data while using experience to interpret the data is not illicit; an expert need not actively conduct his or her own test to have a valid methodology." *Id.* (internal citations omitted). The Court went on to conclude:

> Corrigan's general methodology—gathering relevant information and applying one's training, experience, and knowledge to a process of analyzing the information is a matter of common sense, and it has been deemed 'reasonable' (and thus, presumably, acceptable) by the Seventh Circuit.

Id. at 743-44 (citing *Clark*, 192 F.3d at 758) (internal citations omitted). The same is true here: Goldstein married data he compiled within his own Propecia-patient population against the findings of other clinicians in peer-reviewed studies. This satisfies *Daubert*.

Goldstein's report provides a clinical assessment of common causes of sexual dysfunction in men, and many of the various treatment options. Specifically, he describes common causes of erectile dysfunction that are physical in nature, and includes vasculogenic erectile dysfunction where there are alterations in blood flow to the penis and penile tissue fibrosis. Based upon some of the same clinical and scientific data that Traish considered, Goldstein offers his opinion that finasteride therapy (5α-reductase inhibition) can cause persistent suppression of 5α-reductase which, in turn, leads to a state of androgen deprivation: a) causing biochemical changes in

cavernosal tissue; b) impacting tissue material properties; and c) resulting in clinical impacts stemming from these changes. Merck does *not* challenge this aspect of his report.

B. Gray-scale Ultrasound Imaging is an Accepted Scientific Method in Observing and Measuring Penile Fibrosis.

The use of gray-scale ultrasound imaging—the very tool Goldstein employed to observe and measure penile fibrosis in his patients—is well settled. Merck does not dispute this. In fact, its own expert concedes that duplex ultrasonography is a tool used to "measure vascular flow, cavernous smooth muscle content, calcification and/or plaque formation."[28] That is because "[ultrasonography] is the primary imaging modality in patients with penile disease."[29] Importantly, Kalokairinou states:

> Ultrasonography is performed due to its easy availability, low risk, and ability to image and quantify both calcified and soft tissue elements of PD. Additionally, the vascular status can be assessed if it is indicated. It also provides identification of smaller and non-palpable lesions and evaluates the extent of fibrosis. *This information has clinical relevance because sonography can show lesions that precede the formation of classic plaques*.

Id. at 2:66 (ECF p. 4) (emphasis supplied). In fact, in 2017 Goldstein presented on this very same issue (diagnosing ED via gray-scale ultrasound in over one hundred of his patients) at the 32nd Annual Meeting of the Engineering and Urology Society. *See Laszlo Aff.*, Ex. 52. Ultimately, the abstract received the "Top 10 Abstract" award. *Id.* Moreover, he is not alone in concluding that gray-scale ultrasound imaging is an important diagnostic tool. As noted above, *Merck's own expert*—championed the use of gray-scale. Of course, Merck knows this, which is why its argument does not attack Goldstein's use of gray-scale ultrasound imaging; but rather, objects to the conclusions he reached after interpreting the data. In short, Merck does not like what Goldstein

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[28] *Laszlo Aff.*, Ex. 31 at 1, Punjani, N; Stern, N.; ***Brock, G***. *Atypical Peyronies – A Common Clinical Population That Remains Unrecognized*.

[29] *Laszlo Aff.*, Ex. 51 at 4, Kalokairinou, K. *US Imaging in Peyronie's Disease.* JOURNAL OF CLINICAL IMAGING SCIENCE, 2:66.

saw in the gray-scale ultrasound images. This is not the stuff of a proper *Daubert* challenge; it is the stuff of cross examination.

C. Harmonious Gray-scale Image Readings Between Goldstein and Dr. Bertolotto.

To quibble with Goldstein's finding, Merck glosses over relevant testimony *and* data Goldstein submit to Dr. Bertolotto ("Bertolotto")—a researcher from Trieste, Italy—for review. Specifically, Merck argues Bertolotto disagrees with Goldstein's scoring categories in "52% of the *27 Propecia-exposed subjects*." *Defs' Brief*, Dkt. No. 111 at 30 (emphasis supplied). At the outset, commenting on the reliability of gray-scale imaging Bertolotto wrote: "The good new[s] is that results *are highly consistent*, so, this kind of evaluation likely works, and, although subjective, it is reproducible!" *See Laszlo Aff.*, Ex. 53 at 1 (emphasis supplied). More important, the ability to replicate his results was in reality *confirmed* by Bertolotto's subsequent review. Specifically, the number of subjects Goldstein and Bertolotto reviewed was 37, *not* 27. A control group of 10 individuals were reviewed in addition to 27 Propecia-exposed individuals. *Id.*, Ex. 54. While Merck questioned Goldstein at length regarding the control group, any inclusion of them in its calculations as to the agreement percentage between Bertolotto and Goldstein is conspicuously missing in its brief. In reality, 37 individuals were reviewed. This number is significant because it directly impacts the mathematical games Merck attempts to play.

Based on this intentional exclusion, during his deposition Goldstein specifically supplanted Merck's attempt to misconstrue the data:

> Q. So that—so in terms of the—in terms of what the interpretation was, you and Dr. Bertolotto disagreed 52 percent of the time. Fair?
>
> A. No. It is not fair. It is completely—it is completely inappropriate. What is appropriate here is a differential diagnosis of how to manage the patient. And the patient—Dr. Bertolotto and I—as soon as Bertolotto said anything that he has corporal fibrosis, we have 100 percent agreement.

> You can make all the numbers you want. They are just games. [. . .] For you to say here that we disagree on moderate and moderate to severe is—it is just so clinically silly that it's—I don't even want to go there anymore.[]

Id., Ex. 48 at 595:25-596:21. Worse, the two columns Merck focused on to determine whether there was "agreement" were actually a means to track whether fibrosis was present at all—not the degree of fibrosis specifically. *Id.* at 710:12-18.

Reviewing all of the data yields vastly different results than Defendants' "52%." *Id.* at 711:3-715:16. Of the 27 Propecia-exposed individuals, Bertolotto and Goldstein agree that fibrosis is present in 21 out of 27 individuals. *Id.* at 711:3-713:10; *see Laszlo Aff.*, Ex. 55. Of the 10 control group individuals, no fibrosis is present, and agreement is 100%.[30] *Id.* at 714:7-20. In sum, there is agreement on 31 of 37 individuals as to the presence of fibrosis—or approximately 84%. *Id.* at 714:23-715:10. In all, Merck does not challenge Goldstein's qualifications, the prevalence and acceptance of gray-scale ultrasound imaging, *or* Goldstein's ability to interpret the images. Merck simply does not like Goldstein's conclusions. This is not excludable testimony under *Daubert*; rather, it relevant testimony subject to vigorous cross-examination *at trial*.

III. DR. ETMINAN IS NOT A "BIASED" WITNESS; HIS RESULTS ARE METHODOLOGICALLY SOUND.

Merck contends Etminan's testimony should be struck because: 1) he is a "experienced" witness who is purportedly "biased"; 2) that his work is unreliable, despite being published (twice) in peer-reviewed literature; and 3) his methodology related to certain studies is flawed.

A. Etminan is Qualified to Testify in this Case.

Etminan is an assistant professor in the Department of Medicine, Ophthalmology Division at the University of British Columbia. *See Laszlo Aff.*, Ex. 56. He has twenty years of experience

[30] While 2 of the 10 individuals were classified as "none/mild" by Bertolotto, Goldstein interprets this to mean "none." *Laszlo Aff.*, Ex. 48 713:19-714:6.

as a clinical pharmacologist and epidemiologist. *Id*. For more than fifteen years, he has conducted and published drug safety studies. *See Defs' Decl.*, Dkt. No. 111-1, Ex. 9 at 1, 2. He has acted as a consultant to drug regulatory agencies, including FDA, Health Canada, and EMEA. *Id.* He has more than one hundred published articles in the area of drug safety and serves as a reviewer for journals in this area. *Id*. Etminan is well-credentialed in the area of drug safety.

In fact, at least one other district court tacitly endorsed his qualifications to render the type of work he did in this litigation. In *In re: Fosomax,* Etminan offered an epidemiological review predicated upon the Bradford-Hill criteria. Ultimately, the Court excluded his testimony (in part) because he lacked experience in formulating epidemiological opinions predicated upon the Bradford-Hill criteria. In doing so however, the court specifically said the following:

> In his report, Dr. Etminan arrives at his general causation opinion after applying a Bradford Hill analysis based upon his review of much of the evidence described above-case reports, case series, prevalence studies, and animal studies. *This is not the methodology that he usually follows in his professional work. He testified that his expertise is in observational epidemiology. (07/09/09 Hrg. Tr. at 88.) His work focuses on conducting controlled studies using large administrative databases to determine* the relative risk between an exposure and a rare adverse event. (*Id.* at 88-89; Etminan Rep. at 1.)

In re Fosamax Prod. Liab. Litig., 645 F. Supp. 2d at 187-88 (emphasis added). In this case, however, Etminan did precisely what he does in his day to day research, and precisely what the *Fosamax* Court explained he should have done in that case; namely, a large-scale study based on an administrative database. *See Defs' Decl*., Dkt. No. 111-1, Ex. 9 at 4.3. Moreover, his work was subject to the scrutiny of the peer-review process and published in a prestigious journal. Simply stated, Judge Keenan suggested that *had* Etminan performed a large-scale data-base review to ascertain an HR ratio, his testimony very well may have satisfied *Daubert*. That is precisely what he did in this case—a large scale database review.

B. While Etminan is Ostensibly "Experienced" in Litigation, that "Experience" does not Create a Litigation Bias in this Case.

Merck goes to great lengths to paint Etminan in an unfavorable light as someone who endeavored to create a cottage industry working for plaintiffs in litigation against the pharmaceutical industry. This is simply untrue. At the outset, this is only the *third case* in the past ten years where he agreed to serve as an expert. Specifically, he provided expert testimony in *two—and only two—* prior cases (Fosamax and Mirena). *See Laszlo Aff.*, Ex. 57 at 14:7-15:20.[31] Offering an expert opinion for the third time in ten years cannot alone be the basis for excluding his testimony as unreliable. More important, *even if* Etminan had concocted a cottage industry to gin-up favorable pro-plaintiff opinions, that fact—which is far from proven—is utterly irrelevant here.

Etminan has published *three separate* articles on finasteride. He did his first study in 2013—nearly three years *before any* lawyer ever contacted him.[32] Of course, Merck does not quibble with the results of that study. That may be because he reached a pro-Merck opinion concluding that there was no epidemiological basis to link breast cancer to finasteride consumption. The obvious "analytic gap" Merck's quasi-endorsement of this study has on its bias theory notwithstanding, the argument fares little better when evaluating Etminan's later work. Specifically, he undertook his second analysis in 2015, *more than a year before* being retained by Plaintiff's Counsel.[33] In fact, he testified the idea for the second study came from his co-author who worked at Eli Lilly & Co. who was interested in evaluating whether the FAERs database

[31] Etminan was deposed in Abilify and Risperdal—but he did not serve as an expert witness. He had consulted with plaintiff's counsel in both cases, but was deposed simply a third-party fact witness. *See Laszlo Aff.*, Ex. 57 at 17:8-18:20. In fact, in Abilify he was never hired or received any payment.

[32] *Laszlo Aff.*, Ex. 58 Bird ST Brophy JM Hartzema AG Delaney JA Etminan M. *Male breast cancer and 5α-reductase inhibitors finasteride and dutasteride*. J UROL. 2013 Nov, 190(5):1811-4.

[33] *See Defs' Decl.*, Dkt. No. 54111-1, Ex. 49, Ali AK Heran BS Etminan M. *Persistent Sexual Dysfunction and Suicidal Ideation in Young Men Treated with Low-Dose Finasteride: A Pharmacovigilence Study*. PHARMACOTHERAPY. 2015 Jul; 35(7):687-95; *See Laszlo Aff.*, Ex. 57 at 38:8-10, 39:18 – 41:6 (noting he was retained in 2016).

evidenced a safety-signal associating finasteride with persistent sexual dysfunction. *Id.* at 162:11-24. In his third paper—which was published *after* he was retained—he testified that most of the protocol for *Guo* was completed by the time he was retained.[34] Additionally, in that peer-reviewed publication (where he identified an elevated HR for finasteride and persistent sexual dysfunction) the article *specifically noted* he was a *paid expert in this case* and yet, it was still published.

Further, a cursory review of his prior litigation experience establishes that his two prior forays into the world of litigation were substantially different than that in this case. Approximately ten years ago, Etminan served as an expert in the *Fosamax* litigation, notably against the same Defendant here. It was the first time he offered an opinion as an expert witness. In that case—unlike here—he was not asked to do any independent research regarding Fosamax and did not publish any of his analysis in the peer-reviewed literature. Similarly, his assignment tasked him with providing an opinion that was outside his normal area of expertise.[35]

The second time Etminan acted as expert was in the Mirena IUD litigation. In that instance, he was asked to analyze FDA adverse event reports. Ultimately, he did an analysis and provided a report, but concluded there were errors in his work. Following that realization, he alerted the lawyers in the case of his concerns and withdrew as an expert. As he testified, he did not believe the science was available to allow him to proceed as an expert noting, "I didn't think I could add any more value as an epidemiology expert in that case." *See Laszlo Aff.*, Ex. 57 at 16:2-5; 16:21-17:1. Simply stated, he realized that he could not continue to support a finding of causation, and acting with integrity, withdrew from the litigation.

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[34] *Laszlo Aff.*, Ex. 57 at 41:7-23; *See Defs' Decl.*, Dkt. No. 54111-1, Ex. 48, Guo M Heran B Flannigan R Kezouh A Etminan M. *Persistent Sexual Dysfunction with Finasteride 1 mg Taken for Hair Loss*. PHARMACOTHERAPY. 2016 Nov; 36(11): 1180-1184.

[35] And even then, the court still allowed him to testify on the limited topic of detecting rare adverse events in clinical trials meaning, at a minimum, he was found to be a qualified expert.

Etminan's three experiences as a testifying expert do not remotely rise to the level of undue bias that necessitates exclusion. Exclusion of expert testimony due to litigation bias is an extreme result. *See, e.g., In re Welding Fume Prods. Liab. Litig.*, 534 F. Supp. 2d 761, 766 (N.D. Ohio 2008). For example, in *McClellan v. I-Flow*, the Court excluded the expert's testimony because the plaintiffs retained the expert before he undertook the study, provided all the data to the expert, and the expert conceded he had no experience with the subject matter of his study. *McClellan v. I-Flow Corp.*, 710 F. Supp. 2d 1092, 1120-22 (D. Or. 2010). Here, Etminan published three articles on finasteride (two prior to being retained and one where he specifically disclosed his work on behalf of plaintiff's lawyers). In each case, he was solely responsible for accumulating, analyzing and commenting upon the data. *See Laszlo Aff.*, Ex. 57 at 37:24-38:20. It is hardly surprising that plaintiff's lawyers would reach out to a scientist following his independent publications or that his expert report would incorporate his prior peer-reviewed work. In any event, there is simply no basis to suggest—let alone prove—that his work was concocted in the hopes he would later be retained (particularly given one article is adverse to plaintiffs). What is clear is that his publications (including *Ali* and *Guo*) satisfied the rigors of the peer-reviewed process. As such, they meet the *Daubert* criteria. *See Daubert II*, 43 F.3d at 1317.

C. Etminan's Report and Opinion are Predicated on a Reliable Methodology.

As with its attack on Plaintiff's other experts, Merck ignores large swaths of his report, focusing instead on piecemeal attacks of individual articles. For example, *nothing* in Merck's brief questions the meta-analysis Etminan performed, suggests that meta-analysis is not a viable tool, or contends he did his meta-analysis incorrectly. *See Defs' Brief*, Dkt. No. 111 at 36. Instead, Merck points to his discussions of individual articles within his global opinion in an effort to portray his report as unreliable. *Id.* at 37-43. Daubert challenges, however, must be predicated on

the method the expert employed to reach his conclusion. *See Daubert*, 509 U.S. at 579. Where, as here, the attack is based on the expert's interpretation of a particular article or data-point, the argument is one that challenges the weight of the opinion as opposed to the merit of the methodology. *See In re Digital Music Antitrust Litigation*, 321 F.R.D. 64, 79 (S.D.N.Y. 2017) (citing *Campbell v. Metro. Prop. & Cas. Ins. Co.*, 239 F.3d 179, 186 (2d Cir. 2001)) ("To the extent that Plaintiffs wish to dispute the interpretation of this evidence, a Daubert motion is an inappropriate stage in the litigation to do so."). This type of challenge falls squarely within the realm of cross examination. *See Olin Corp. v. Certain Underwriters at Lloyd's London*, 468 F.3d 120, 134 (2d Cir. 2006). Here, Etminan's opinions rests not only on his own work in *Ali* and *Guo*, but also on his meta-analysis of papers from within the medical literature establishing an elevated HR linking finasteride to persistent sexual dysfunction.[36] Experts routinely rely on multiple studies, which considered separately may not alone establish causation, but together have probative value. *See* REFERENCE MANUAL ON SCIENTIFIC EVIDENCE (THIRD) Sec. III.B (2011). As such, while any individual study may have flaws, an opinion that evaluates the cumulative information and the totality of circumstances falls squarely within the realm of acceptable expert opinion. *See Drake*, 111 F. Supp. 3d at 567 (D. Vt. 2015) appeal dismissed (Nov. 12, 2015).

Drake is instructive. In *Drake*, the court allowed the expert to testify notwithstanding the fact the court concluded certain aspects of the report were predicated on a purported "analytical gap." *Id.* at *568. The court reasoned the combination of the expert's reliance on published medical literature, and the totality of evidence, coupled with a viable theory on biological plausibility left any "analytical gap" for cross-examination. *Id.* at 568. The same is true here. Here, Etminan relied on no less than eight peer-reviewed articles to complete his meta-analysis. Ostensibly recognizing

[36] *See Defs' Decl.*, Dkt. No. 54111-1, Ex. 49 (*Ali, et al.*, 2015), and Ex. 48 (*Guo, et al.*, 2016).

as much, *nothing in Merck's brief* challenges his meta-analysis from a methodological perspective. Instead, Merck argues *his interpretation* of certain studies is wrong. That is not a basis to exclude an expert's opinion; it is, instead a basis for cross-examination. As in *Drake*, the fact some pieces of evidence include technical flaws or imperfections, is not a basis to exclude the testimony. *Drake* at 568. [redacted] *Supra* at 7. [redacted] *Id.* The combination of his meta-analysis, [redacted] and Traish's theory on biological mechanism are more than sufficient to satisfy *Daubert*. With that backdrop, Plaintiff now responds to Merck's critiques.

1. Critique No. 1: His opinions on persistence are expressed in his Report and published work and as such, are reliable and should be allowed.

Merck initially claims, "Nowhere in his Rule 26 report does Etminan state that Propecia is responsible for sexual side effects that occur during drug use and persist after discontinuation." *Defs' Brief*, Dkt. No. 111 at 36. This is simply not true. His report expressly concludes: "Based upon my published work on a large clinical database, finasteride is linked to long term SD effects after use of the 1 mg dose in certain men." *See Defs' Decl.*, Dkt. No. 111-1, Ex. 9 at 4.3. In fact, the *Guo* publication is titled *Persistent Sexual Dysfunction with Finasteride 1mg*. *Id.*, Ex. 48. His report and deposition clearly evidence his view that finasteride causes persistent SAEs.

2. Critique No. 2: Bradford Hill is not required in order to offer an opinion on causation.

There is simply no definitive requirement that an epidemiologist employ the Bradford Hill criteria in order to reach a determination of causation. *In re Neurontin Marketing, Prod. Liab.*

Litig., 612 F. Supp. 2d 116, 131-34 (D. Mass. 2009) (the court reasoned that Bradford Hill was merely one approach to establishing causation). Furthermore, the court noted that while several courts have recognized the Bradford Hill criteria as a tool for determining epidemiological causation, other courts have found the Bradford Hill criteria neither "necessary [n]or helpful." *Id.*at 133 (citing *In re Phenylpropanolamine (PPA) Prods. Liab. Litig.*, 289 F. Supp. 2d 1230, 1243 n.13 (W.D. Wash. 2003)); *Dunn v. Sandoz Pharms. Corp.*, 275 F. Supp. 2d 672, 678 (M.D.N.C. 2003) (same) (collecting cases). In short, there is simply no requirement an epidemiologist utilize the Bradford Hill criteria in order to render a causation opinion.

3. Critique No. 3: Ali is not unreliable because of MedDRA terms – it is the same analysis Merck performed to look at the same thing.

Merck attacks *Ali* claiming his work was flawed. At the outset, the *Ali* study—published more than a year *before* Etminan's retention—was accepted for publication in a well-respected peer-reviewed journal. The mere fact it was published *before* litigation is evidence it is not "junk science." *See Daubert II*, 43 F.3d at *1317. Recognizing as much, Merck identifies a handful of MedDRA reports it claims were improperly included in the analysis. *Defs' Brief*, Dkt. No. 111 at 37-39. Even if that is true, the purported improperly included reports merely go to the weight, as opposed to the reliability of the conclusion. *See Zerega Ave. Realty Corp v. Hornbeck Offshore Transp. LLC*, 571 F.3d 206, 214 (2d Cir. 2009) (quoting *Boucher v. U.S. Suzuki Motor Corp.*, 73 F.3d 18, 21 (2d Cir.1996)) ("that the assumptions are unfounded go to the weight, not the admissibility, of the testimony"); *accord Arista Records LLC v. Lime Grp.* LLC, No. 06 CV 5936(KMW), 2011 WL 1674796, at *3 (S.D.N.Y. May 2, 2011).[37]

[37] [redacted]

Equally important, Merck's attack on *Ali*—i.e., that Ali inaccurately reviewed the data—is, at best highly speculative, if not altogether misleading. *Defs' Brief*, Dkt. No. 111 at 37-39. During his deposition Etminan testified he did not know what Ali reviewed. Reliance on mere speculation—as Merck does here—is, of course, precluded by Rule 602 of the Federal Rules of Evidence.[38] Underscoring that point, Etminan specifically testified that Ali analyzed the MedDRA reports, as such, he had no way to knowing if the reports he was shown in deposition were *ever* included, let alone whether Ali had even seen them. *See Laszlo Aff.*, Ex. 57 at 166: 20-25; 169:9-22; 227:18-23. A defendant's critique that is based on little more than rank speculation is, in the end, no attack at all. *See In re Zyprexa Prods. Liab. Litig.*, 489 F. Supp. 2d 230, 285 (E.D.N.Y. 2007) (citing *Daubert*, 509 U.S. at 594, 113 S.Ct. at 2797)) ("Expert testimony should not be rejected simply because the conclusions reached by the witness seem subjectively improbable."). Merck (literally) had years to depose Ali. It chose not to do so. Accordingly, any speculation on what Ali did or did not do, does not outweigh the fact the paper was accepted for publication in a peer-reviewed journal; the hallmark of reliable scientific evidence. *See Daubert II*, at 1318.

4. Critique No. 4: Guo adjusted for confounders and is reliable.

Etminan's 2016 publication (*Guo*) evidenced a risk of persistent sexual dysfunction following use of finasteride. Merck claims the study is unreliable because it "involves an analysis of sexual dysfunction events occurring only after finasteride was discontinued, regardless of whether sexual dysfunction either existed before drug use or first occurred during drug use." *See Defs' Brief*, Dkt. No. 111 at 4. In *Guo*, the researchers analyzed three groups of men. *See Laszlo Aff.*, Ex. 57 at 241:6-242:6. The first group consisted of men who stopped finasteride and then had a sexual event outcome. *Id.* The second group consisted of men who stopped finasteride and later

[38] As such, Plaintiff's Counsel raised an objection to the exhibit and any testimony as it relates to those forms is speculative at best and these arguments fail. *Id.*, Ex. 57 at 226.

filled a prescription for a PDE5 inhibitor (e.g., Viagra). *Id*. The third group evaluated men who experienced ED six months into their treatment with finasteride and continued to experience ED for six months post-use. *Id*. Merck's criticizes the study contending Etminan failed to consider whether the SD existed before drug use. This is not an accurate reflection of his work.

Specifically, Etminan testified, his research team did not want to exclude certain patients "[b]ecause we would have eliminated our sample and we would have lost power, so adjusting would be the same as excluding." *Id.*, at 276:1-277:6. In short, the team reasoned it needed the men it included to adequately power the study. But, *even if* the study included some small number of men who experienced erectile dysfunction prior to starting finasteride it is of no moment because perfection is not required. Quoting the Third Circuit, the *Graham* court observed:

> The grounds for the expert's opinion merely have to be good, *they do not have to be perfect.* The judge might think that there are good grounds for an expert's conclusions even if the judge thinks that there are better grounds for some alternative conclusion, *and even if* the judge thinks that a scientist's methodology has some flaws such that if they had been corrected, the scientist would have reached a different result.

See Graham, 993 F. Supp. at 133 (emphasis supplied). Here, Etminan's opinion may not be "perfect." However, his justification for his work—i.e., why he opted to include the men he included in his study—are justifiable.[39] In fact, absent from Merck's critique was Etminan's testimony that he considered the issue *and adjusted for it* in his analysis. Accordingly, any "flaw" in the data is not fatal to his methodology, but instead goes to the weight of his testimony.

IV. GOLDSTEIN'S CASE SPECIFIC CAUSATION OPINION AS TO PLAINTIFF DAWSON IS ADMISSIBLE.

[39] Addressing Merck's critique, Etminan said the following: "If you look at page 1183, a similar covariate adjustment approach was used for the secondary analysis. So we basically looked—we used the same covariates in the table in the adjusted model and we presented in table 4." *Laszlo Aff.*, Ex. 57 at 277:2-6.

Merck seeks to exclude Goldstein's case-specific opinion that Propecia caused Paul Dawson's ("Dawson's") sexual dysfunction. The Court ought to deny that motion because: 1) the general causation opinions are reliable and buttress his case-specific observations; and 2) Goldstein's case specific causation opinion is based on a proper differential diagnosis, which the Second Circuit recognizes satisfies *Daubert*. [40]

A. A Brief Overview of Dawson's Medical Treatment.

Dawson used Propecia from February 2008 to June 2008. *See Defs' Decl.*, Dkt. No. 111-1, Ex. 54. He began experiencing sexual side effects while on Propecia. *See Laszlo Aff.*, Ex. 61. Shortly thereafter, he saw Dr. Michael Valbuena, his primary care physician, on June 16, 2009 complaining of sexual side effects related to Propecia. *Id.*, Ex. 62 at 201-203; *see Defs' Decl.*, Dkt. No. 111-1, Ex. 55 at 3. During the course of his treatment, Dr. Valbuena performed a complete physical examination. *Laszlo Aff.*, Ex. 63 at 39:18-25; 40: 1-25; 41: 1-25; 42:1-25; 43: 1-25; 44:1-25; 45:1-20. Specifically, he ordered lab work to check Dawson's thyroid levels, testosterone levels, and prolactin levels. *Id*. at 63:23-25; 63:1-2.

On October 5, 2016, Goldstein performed a Rule 35 Independent Medical Examination of Dawson. *See Defs' Decl.*, Dkt. No. 111-1, Ex. 55. In connection with this visit, Goldstein reviewed Dawson's medical records, including Dr. Mah's February 13, 2008 record setting forth her discussion with Mr. Dawson addressing the Propecia SAEs identified by Merck, the drug manufacturer, and performed his own tests and examinations, including an ultrasound of Dawson's

[40] Even in the absence of general causation, a differential diagnosis alone may establish both general and case specific causation. "[A]ccording to the Second Circuit, if a qualified expert performs a reliable differential diagnosis, the plaintiff need not satisfy the general causation requirement." *See Plourde v. Gladstone*, 190 F. Supp. 2d 708, 722 n.7 (D. Vt. 2002); *see also McCullock v. H.B. Fuller Co.*, 61 F.3d 1038, 1043-44 (2d Cir. 1995) (district court did not abuse discretion in ruling that opinion on causation was admissible, where opinion was based on care and treatment of plaintiff, medical history, pathological studies, product's safety data sheet, reference to scientific and medical treatises, expert's training and experience, as well as differential diagnosis).

penis that revealed fibrosis. Goldstein's differential diagnosis led to his opinion that finasteride was the cause of Mr. Dawson's sexual dysfunction. *See Defs' Decl*., Dkt. No. 111-1, Ex. 55 at 7, Ex. 64 at 361:4-15.

B. Goldstein's Differential Diagnosis that Finasteride is the Cause of Dawson's Injuries is Reliable.

Dr. Goldstein performed differential diagnoses in order to determine the cause of Dawson's sexual dysfunction. A differential diagnosis is a patient-specific process of ruling out potential causes of an injury as unlikely until the most likely cause remains. *See Ruggiero v. Warner–Lambert Co*., 424 F.3d 249, 251 (2d Cir. 2005). In the Second Circuit, a case specific expert who performs a differential diagnosis satisfies the *Daubert* standard and should not be excluded. *Id*.; *see also McCullock*, 61 F.3d at 1044 (disputes about an expert's use of differential diagnosis "go to the weight, not the admissibility, of [the expert's] testimony"). Merck's attack on Goldstein's differential diagnosis comes down to essentially one argument: specifically, Merck argues Dawson's sexual dysfunction is psychological in origin and claims Goldstein failed to consider this in his differential diagnosis. This is clearly not the standard and clearly not the facts in this case.

1. Goldstein's differential diagnosis includes penile fibrosis—which cannot be caused by psychological factors.

When Dawson visited Goldstein in San Diego, Goldstein performed an ultrasound which revealed fibrosis of his penile tissue. *See Defs' Decl., Dkt. No. 111-1, Ex. 55* at 6, Ex. 64 at 361:4-15. The physical scarring of penile tissue cannot occur via a psychological issue. As Goldstein testified, "you don't make up corporal fibrosis." *See Laszlo Aff.*, Ex. 64 at 451:5. Because there is physical evidence of fibrosis in Dawson (and the penile fibrosis theory is valid

science as detailed throughout this brief) Goldstein has provided a reliable differential opinion as to his injuries.

2. Even if there was an absence of fibrosis, Goldstein's differential diagnosis is reliable, and establishes that finasteride caused Dawson's injuries.

Merck's seeks to exclude many of Goldstein's opinions as they relate to his reading of Dawson's gray-scale imaging. Even if this Court were to exclude his opinions as they relate to gray-scale imaging and his findings of fibrosis in Dawson, Goldstein offered a reliable differential diagnosis concluding finasteride caused his injuries. *See Defs' Decl.*, Dkt. No. 111-1, Ex. 55 at 5. Goldstein's evaluation included review of Dawson's treating physician records and testimony, along with his own which is sufficient to establish causation.

The cases Merck cites from this Circuit excluding experts based on the failure to perform a reliable differential diagnosis are readily distinguishable. *See, e.g., Ruggiero v. Warner-Lambert Co.*, 424 F.3d 249, 254-55 (2d Cir. 2005) (where the expert's differential diagnosis was insufficiently reliable to support an opinion as to *general causation* because the expert did not show that the drug was capable of causing the injury; while the expert ruled out some possible causes, the expert did not *rule in* the drug as one of possible causes through scientifically valid methodology, *i.e.*, the expert could not point to *any* studies suggesting that the injury could be caused or exacerbated by the drug).[41] Here, Goldstein did consider alternative causes to form his

[41] *See also In re Mirena IUD Prods. Liab. Litig.*, 169 F. Supp. 3d at 459 (expert opinions were excluded as unreliable for being based purely on speculation, and further, the expert did not consider alternate causes that may have caused the injury of perforation); *In Re Fosamax Prods. Liab. Litig.*, 924 F. Supp. 2d at 493 (where the Court held an expert's opinion as to causation was inadmissible because the expert testified that he could not say whether the drug was or was not the cause of the plaintiff's jaw injury); *Morritt v. Stryker Corp.*, 973 F. Supp. 2d 177, 189-91 (E.D.N.Y. 2013) (where the doctor's differential diagnosis was excluded because, in part, because the doctor speculated as to the facts, provided no scientific foundation for conclusions, and was not qualified to rule in or rule out causes); *Munafo v. Metropolitan Transp. Authority*, 00-CV-0134 (ERK), 2003 WL 21799913, at *18 (E.D.N.Y. Aug. 4, 2003) (where the doctor admitted in his deposition that he made no attempt to perform a differential diagnosis as to the cause of the plaintiff's depression); *Plourde v. Gladstone*, 190 F. Supp. 2d 708, 722-23 (D. Vt. 2002) (doctor's opinion to find general causation was inadmissible as the expert relied on other doctors findings that offered no opinions that could be used to make an inference as to causation, and failed to exclude other likely possible causes).

opinion, along with the temporal relationship of the symptoms and the medical literature as identified in his general causation opinion. *Infra* at 48-49.

3. Goldstein did consider psychological issues as a cause of Dawson's sexual dysfunction and ruled it out.

Merck improperly characterizes Goldstein's opinion so as to suggest he did not properly consider the potential psychological overlay that may contribute to Dawson's sexual dysfunction. Goldstein considered the records and his examination and testing in forming his opinions in concluding that Dawson's impotence *was not* of psychological origin. *See Laszlo Aff.*, Ex. 64 at 442:11-23. An expert can rely on the contemporaneous records of the treating doctor's to reliably testify on an issue. *See Blake v. U.S.*, No. 10-CV-610S, 2017 WL 1371000, at *7 (W.D.N.Y. April 17, 2017). Further, Goldstein testified that he considered the psychological component when forming his opinion, stating "I do not believe it's psychologic, primarily, dysfunction." *See Laszlo Aff.*, Ex. 64 at 394:6-13. Merck's disagreement with the weight he gave to this issue, does not mean he failed to consider it.

4. Goldstein need not consider every possible cause in order for his opinion to be reliable.

Even if the Court were to agree with Merck that Goldstein did not properly consider the potential psychological issues as a cause of Dawson's sexual dysfunction, that alone is not a sufficient basis to exclude his testimony. "A medical expert's opinion based upon differential diagnosis normally should not be excluded because the expert has failed to rule out every possible alternative cause of a plaintiff's illness." *Davids*, 857 F. Supp. 2d at 278 (quoting *Cooper v. Smith & Nephew, Inc.*, 259 F.3d 194, 202 (4th Cir. 2001)). Further, "[w]hile an expert *need not rule out every potential cause* in order to satisfy *Daubert*, the expert's testimony must at least address obvious alternative causes and provide a reasonable explanation for dismissing specific alternate

factors identified by the defendant." *See Israel v. Spring Indus*., No. 98 Civ. 5106, 2006 WL 3196956, at *5 (E.D.N.Y. Nov. 3, 2006) (emphasis supplied); *DeRienzo v. Metro. Transp. Auth.*, 694 F. Supp. 2d 229, 236 (S.D.N.Y. 2010).

Adeghe v. Janssen Pharm., Inc., No. 16 CIV. 2235 (LGS), 2017 WL 3741310 (S.D.N.Y. Aug. 30, 2017), reconsideration denied, No. 16 CIV. 2235 (LGS), 2017 WL 4839063 (S.D.N.Y. Oct. 24, 2017), is instructive. *Adeghe* involved a product liability action involving the drug, Risperdal. In *Adeghe*, the defendant argued the case specific expert opinion was unreliable because the expert did not consider the entirety of the plaintiff's medical history. Nonetheless, the court held that even if a doctor did not review complete medical records, it did not render the testimony as inadmissible. *Id.* at *4. Using this criteria, even if Goldstein did not review Dr. Hartzell's ("Hartzell") records, it does not make his testimony inadmissible. That is particularly true here, given he testified he *did* consult with Hartzell on her findings. *See Laszlo Aff.*, Ex. 64 at 390:22-25; 391: 1-4. Goldstein's report clearly satisfies this threshold, as he specifically ruled out diabetes, high blood pressure, and other hormonal issues. *See Defs' Decl*., Dkt. No. 111-1, Ex. 55 at 7. Further, he relied upon the testimony and records of Dawson's treating physicians, who as detailed above, also conducted a differential diagnosis to rule out other possible causes of erectile dysfunction—including their belief Dawson's sexual dysfunction *was not* psychological. In fact, to date, no actual physician treating Dawson has attributed his persistent sexual dysfunction to be psychological in origin.

In addition to ruling out other causes of Dawson's sexual dysfunction, Goldstein found the temporal relationship of the symptoms to be compelling evidence of causation. The Second Circuit has allowed expert testimony to proceed to the jury where the opinion relied, in part, on the progression and timing of the development of a disease to support an inference of causality. *See*

Zuchowicz v. United States, 140 F.3d 381, 390 (2d Cir. 1998); *see also Westberry v. Gislaved Gummi AB*, 178 F.3d 257, 265 (4th Cir. 1999) (explaining that under some circumstances "a temporal relationship between exposure to a substance and the onset of a disease or a worsening of symptoms can provide compelling evidence of causation"); *Heller v. Shaw Indus., Inc.*, 167 F.3d 146, 154 (3d Cir. 1999) (noting courts "have looked favorably on medical testimony that relies heavily on a temporal relationship between an illness and a causal event"). Here, Dawson experienced an SAE on drug (an admitted and known risk) that temporally persisted post-use. The temporal nexus of this harm to cessation of Propecia, along with Goldstein's assessment, is more than sufficient to allow him to testify in this case. Goldstein offered an opinion that the most likely cause for Dawson's erectile dysfunction was his use of Propecia. His differential diagnosis is satisfactory and reliable, and his opinion as to case specific causation should be admissible.

CONCLUSION

For the foregoing reason, Plaintiff respectfully requests the Court deny Merck's motion in its entirety.

Dated: December 27, 2017

Respectfully submitted,

/s/ Theodore E Laszlo, Jr.

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CERTIFICATE OF SERVICE

I, Theodore E Laszlo, Jr., attorneys for Plaintiff, do hereby certify that I have this day caused the foregoing to be electronically filed with the Clerk of the Court using the ECF system

which sent notification of such filing to all registered attorneys. Courtesy copies of the documents filed Under Seal Documents and Unredacted Materials have been provided to Merck's Counsel by way of electronic correspondence.

SO CERTIFIED this, the 27th day of December, 2017.

/s/ Theodore E Laszlo, Jr.
Theodore E Laszlo, Jr.